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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,125	09/11/2003	Mark Robert Cobain	T3089(C)	6912

201 7590 09/30/2005

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,125	COBAIN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/11/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/27/04 & 03/29/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the detection of isoprostanes in a biological sample derived from a human, does not reasonably provide enablement for a method of diagnosing a psychological stress level in a human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be

considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of determining a psychological stress level in a human, the method comprising with measurement means, measuring the level of one or more isoprostanes in a biological sample derived from the human and calculating the psychological stress level from the measured isoprostane level. The specification on page 2, lines 3-35 discloses that the presence of psychological stress or increased psychological stress levels can be identified by an increase in the level of one or more isoprostanes. The specification on page 17, lines 24-25 discloses that correlations between urinary isoprostanes and cortisol secreted during stress period for both "stress" and "control groups". Page 18, lines 8-13 disclose that the demonstration that reported perceived stress correlates with the isoprostane levels, and their metabolites, found in urine, and the observation that stress reactivity, as indexed by cortisol secretion occurring during a stress period, is related to the base level of isoprostanes produced indicates that isoprostanes and stress are related.

However, the specification does not clearly teach what is involved in psychological stress or how psychological stress is defined. Further, the specification does not appear to teach a method of diagnosing a psychological stress level in a human. Although, the specification compares cortisol levels of saliva with urine

isoprostanes, the specification does not positively teach diagnosing a psychological stress level in a human by measuring isoprostanes. Nor does the specification disclose a threshold or normal values for patients. Further, according to Taber's Cyclopedic Medical Dictionary, the amount of stress humans can withstand without having a pathological reaction to it varies from individual to individual and from situation to situation.

Also according to Strongin (Laboratory Diagnosis of Viral Infections, Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications, Lennette, e., ed., Marcel Dekker, Inc., New York, pp.211-219, 1992) a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the following: (1) the sensitivity of the assay; (20 the true-positive test rate: (3) the false-negative test rate; (4) the specificity, or percentage of patients without the disease who will display a negative result; (5) the true-negative test rate; (6) the false-positive test rate; (7) the predictive value, or the probability that the test result is correctly indicating the presence or absence of the disease; (8) the prevalence, or number of patients in any given population that have the disease in question; (9) the efficiency or percentage of all results that are true; (10) the accuracy of the recited diagnostic assay.

Additional consideration must also be examined to enable the clinician to practice the invention, including assessment of the following: (1) when is the maximum sensitivity desired? (2) when is the maximum specificity desired?; (3) when is the maximum efficiency desired?; (4) how is the maximum sensitivity or specificity

achieved?; (5) how is the predictive value maximized? An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test.

Because of the lack of description in the specification to diagnose a psychological stress level in a human as claimed and because the specification fails to clearly define psychological stress or teach any information regarding the patients from which the samples were taken, and whether any consideration were given to the disease prevalence, predictive value, efficiency, or accuracy of the recited diagnostic assay, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 the recitation "psychological stress" is vague and indefinite. It is unclear what applicant intends to encompass. The specification does not provide a definition for the phrase.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step of obtaining a biological sample from

the human; also a step positively correlating the measured value of isoprostane to psychological stress level.

Claim 1 is vague and indefinite because it is unclear how the isoprostane is measured.

Claim 1 is vague and indefinite because it is unclear how the psycholocial stress level is calculated from the measured isoprostane level. Does the mere presence of isoprostane, a decrease or an increase of isoprostane indicate psychological stress level? Further, how does one determine if a decrease or an increase has occurred? Is the measured level compared to a standard or control or is applicant detecting levels at different time intervals to determine a change? Please clarify. The specification on page 2, lines 34-35 discloses that the presence of psychological stress or increased psychological stress levels can be identified by an increase in the level of one or more isoprostanes.

Claim 2 is vague and indefinite because it is unclear what applicant intends. Also, it is unclear what relationship exits between the isoprostanes, the level of antibodies and means to measure the antibodies. Please clarify. Does the level of the antibodies correlate with the level of isoprostanes? Is applicant also detecting antibodies in the biological sample or does applicant intend that antibodies are used to detect isoprostanes. Please clarify.

Claim 3 is vague and indefinite because it is unclear how one can determine a psychological stress level in a human if the biological sample comprises more that one body fluid. Is the second body fluid collected from the same individual? Is the second

body fluid collected at the same time or a different time? Is the second body fluid the same type or different from the first biological fluid? Is a correlation established between the first and second biological fluids to determine psychological stress? It is unclear what applicant is trying to encompass.

Claim 5 is vague and indefinite because it is unclear how psychological stress is "associated with" one or more of the recited conditions. It is unclear if applicant is merely stating that psychological stress is related to the recited disorders or if applicant is trying to diagnose the recited disorders. It is unclear what applicant is trying to encompass.

Claim 5 is vague and indefinite because of the use of an acronym: i.e. ME. Although the term may have art recognized meanings, it is unclear if applicant intends to claim the prior art definitions. The term should be defined in its first instance.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-4, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morrow et al (US 5,891,622) in view of Moller et al (Oxidative stress associated with exercise, psychological stress and life-style factors, Chemico-Biological Interactions 102 (1996) 17-36).

Morrow et al disclose methods for determining oxidative stress in an organism by determining the level of isoprostanes in a biological sample and comparing the isoprostane level to a control sample. Morrow et al disclose that the oxidative stress is determined by wherein the amount of isoprostanes increase in the sample isolated from an organism undergoing oxidative stress compared to the control (col 2). Morrow et al disclose that the sample can be a urine sample and can be obtained from a human (col 8 and col 11). Morrow et al disclose that the measuring can be performed using antibodies to the isoprostanes (col 5 – col 6).

Morrow et al differ from the instant invention in failing to teach determining a psychological stress level.

Moller et al disclose that psychological stress increases oxidative stress (abstract and p. 24).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Morrow et al to also determine psychological stress because Moller et al teaches that psychological stress correlates to an increase in oxidative stress. Therefore one of ordinary skill in the art would have a reasonable expectation of success determining psychological stress using the method of Morrow et al because Moller et al shows that oxidative stress is correlated with psychological stress. Further, it is unclear what is meant by the term "psychological stress" (see 112 2nd rejection above). Therefore, for reasons stated above the combination of Morrow et al and Moller et al read on the instantly recited claims.

10. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morrow et al and Moller et al in view of Cohen et al (European Neuropsychopharmacology, Vol 10, Issue 6, Dec. 2000, pgs 429-435).

See above for the teachings of Morrow et al and Moller et al.

Morrow et al and Moller et al differ from the instant invention in failing to teach the psychological stress is associated with post traumatic stress disorder.

Cohen et al disclose that psychological stress is the cause of post-traumatic stress disorder.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recognize that psychological stress is associated with post-traumatic stress disorder because Cohen teaches that psychological stress is the cause of post-traumatic stress disorder. Further, it is unclear how psychological stress is associated with the disorder (see 112 2nd rejection above). Therefore, the combination of Morrow et al, Moller et al and Cohen et al reads on the instantly recited claim.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Roberts, II et al (US 5,858,696) teaches the assessing oxidative stress in vivo by quantification of prostaglandin F2-like compounds and their metabolites.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
September 21. 2005

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